## (19) World Intellectual Property Organization International Bureau



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(43) International Publication Date 20 September 2001 (20.09.2001)

**PCT** 

# (10) International Publication Number WO 01/68836 A3

(51) International Patent Classification<sup>7</sup>: 15/63, C12Q 1/68, A61K 31/7105

C12N 15/11,

(21) International Application Number: PCT/US01/08435

(22) International Filing Date: 16 March 2001 (16.03.2001)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/189,739 60/243,097 16 March 2000 (16.03.2000) US 24 October 2000 (24.10.2000) US

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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

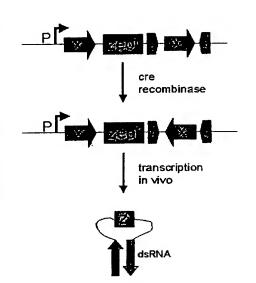
#### Published:

with international search report

(88) Date of publication of the international search report: 14 March 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND COMPOSITIONS FOR RNA INTERFERENCE



(57) Abstract: The present invention provides methods for attenuating gene expression in a cell using gene-targeted double stranded RNA (dsRNA). The dsRNA contains a nucleotide sequence that hybridizes under physiologic conditions of the cell to the nucleotide sequence of at least a portion of the gene to be inhibited (the "target" gene).





Intrational Application No Pui/US 01/08435

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/11 C12N A61K31/7105 C12N15/63C12Q1/68 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) WPI Data, PAJ, CAB Data, SEQUENCE SEARCH, BIOSIS, EPO-Internal C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category ° TUSCHL THOMAS ET AL: "Targeted mRNA 1,9, χ 12-15 degradation by double-stranded RNA in vitro." GENES & DEVELOPMENT, vol. 13, no. 24, 15 December 1999 (1999-12-15), pages 3191-3197, XP002183118 ISSN: 0890-9369 the whole document WO 99 32619 A (CARNEGIE INST OF WASHINGTON Α ; MONTGOMERY MARY K (US); FIRE ANDREW () 1 July 1999 (1999-07-01) the whole document -/--Patent family members are listed in annex. Further documents are listed in the continuation of box C. Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docucitation or other special reason (as specified) O document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means document published prior to the international filing date but later than the priority date claimed in the art. \*&\* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 21/12/2001 16 November 2001 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Hornig, H Fax: (+31-70) 340-3016

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Int<sup>r</sup> tional Application No PC r/US 01/08435

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 29058 A (CARNEGIE INST OF WASHINGTON ;UNIV MASSACHUSETTS (US)) 26 April 2001 (2001-04-26) claims 1-16	1-5,9, 12-15
Р,Х	WO 00 44914 A (FARRELL MICHAEL J ;LI YIN XIONG (US); KIRBY MARGARET L (US); MEDIC) 3 August 2000 (2000-08-03) claims 1-61	1,9, 12-15
Ρ,Χ	BERNSTEIN EMILY ET AL: "Role for a bidentate ribonuclease in the initiation step of RNA interference." NATURE (LONDON), vol. 409, no. 6818, 18 January 2001 (2001-01-18), pages 363-366, XP002183119 ISSN: 0028-0836 the whole document	1-15
Т	HAMMOND SCOTT M ET AL: "Argonaute2, a link between genetic and biochemical analyses of RNAi." SCIENCE (WASHINGTON D C), vol. 293, no. 5532, 2001, pages 1146-1150, XP002183120 ISSN: 0036-8075 figure 3	
Т	MOSS ERIC G: "RNA interference: It's a small RNA world." CURRENT BIOLOGY, vol. 11, no. 19, 2001, pages R772-R775, XP002183121 ISSN: 0960-9822 page R773, right-hand column, line 8 -page R774, right-hand column, line 23	
Т	AMBROS VICTOR: "Dicing up RNAs." SCIENCE (WASHINGTON D C), vol. 293, no. 5531, 3 August 2001 (2001-08-03), pages 811-813, XP002183122 ISSN: 0036-8075 the whole document	
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Int tional Application No
PUI/US 01/08435

		FC1/US U1/U8435		
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
P , X	CAPLEN N J ET AL: "dsRNA-mediated gene silencing in cultured Drosophila cells: a tissue culture model for the analysis of RNA interference" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 252, no. 1-2, 11 July 2000 (2000-07-11), pages 95-105, XP004210158 ISSN: 0378-1119 the whole document	1,9, 12-15		
P,A	HAMMOND SCOTT M ET AL: "An RNA-directed nuclease mediates post-transcriptional gene silencing in Drosophila cells."  NATURE (LONDON), vol. 404, no. 6775, 16 March 2000 (2000-03-16), pages 293-296, XP002183123 ISSN: 0028-0836 the whole document			

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims (2,4-15)-partially (and as far as in vivo methods are concerned) are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Although claims 18 and 19 could be, at least be partially be considered as scheme, rule and method for doing buisness, Rule 39.1(iii) PCT, the search has been carried out as far as possible in our systematic documentation.

Continuation of Box I.2

Claims Nos.: 17

Present claim 17 relate to a method of formulating a pharmaceutical preparation including one or more agents identified by an assay, without giving a true technical characterization. Moreover no such compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

information on patent family members

Int tional Application No PC i /US 01/08435

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9932619	Α	01-07-1999	AU EP WO	1938099 A 1042462 A1 9932619 A1	12-07-1999 11-10-2000 01-07-1999
WO 0129058	Α	26-04-2001	AU WO	1086501 A 0129058 A1	30-04-2001 26-04-2001
WO 0044914	Α	03-08-2000	AU EP WO	2634800 A 1147204 A1 0044914 A1	18-08-2000 24-10-2001 03-08-2000